REMARKS

The present application was filed on April 24, 2001 (claiming priority from United States Provisional Application Number 60/237,590, filed October 3, 2000) with claims 1-28. Claims 4-16, 20-22 and 26-28 have been withdrawn from consideration in response to a previous restriction requirement and are being canceled herein, without prejudice. Claims 1-3, 17-19 and 23-25 are therefore currently pending in the application. Claims 1, 3, 17, 19, 23 and 25 are amended herein merely to clarify the subject matter to which they are directed. Support for the amendment to claims 1, 17 and 23 may be found, for example, in claim 3, as originally filed, and on page 14, lines 9-17 and 24-27, of the specification. Support for the amendment to claims 3, 19 and 25 may be found, for example, on page 14, lines 9-17, of the specification and in FIG. 4.

In the outstanding final Office Action, the Examiner finally rejected claims 1-3 under 35 U.S.C. §101 as allegedly directed to non-statutory subject matter. Specifically, the Examiner stated that the instant claims do not meet the standard of being immediately useful nor is it readily apparent how the results of the method are either concrete, tangible or useful. The Examiner further finally rejected claims 1-3, 17-19 and 23-25 under 35 U.S.C. §101 as allegedly lacking patentable utility. Specifically, the Examiner asserted that the specification lacks any teaching of utility for the claimed method wherein expression signal data is transformed.

The Examiner finally rejected claims 1-3, 17-19 and 23-25 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Namely, the Examiner asserted that the phrase "transformation that renders uniform," appearing in claims 1, 17 and 23, is unclear. The Examiner also asserted that the limitation of rendering uniform a probability distribution, as in claims 3, 19 and 25, is unclear. The Examiner further asserted that the term "mapped," as recited in claims 3, 19 and 25, is unclear.

The Examiner finally rejected claims 1-3, 17-19 and 23-25 under 35 U.S.C. §103(a) as allegedly unpatentable over Eisen, et al. *Cluster Analysis and Display of Genome-*

Wide Expression Patterns, PROC. NATL. ACAD. SCI., vol. 95, pp. 14863-68 (December 1998) (hereinafter "Eisen").

The present invention has been described in Applicants' prior response, incorporated by reference herein.

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FORMAL REJECTIONS

As mentioned above, the Examiner finally rejected claims 1-3 under 35 U.S.C. §101 as allegedly directed to non-statutory subject matter. The Examiner in the final Office Action, beginning on page 2, 4th paragraph, stated that,

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> A method which transforms gene expression signals to find certain
> patterns of expression MAY be one which produces a concrete, tangible, and
> useful result. However, some knowledge is required with regard to a specific
> patterns [sic.] that result from such a method, for example. **In the instant claims,**
> there is no specificity identified as to what is intended by the outcome of the
15
> method. Therefore, the invention does not meet the standard of being
> immediately useful. (emphasis in original)

Applicants respectfully disagree. As Applicants highlighted in their previous response, the present method, e.g., as recited in independent claim 1, can be used to derive a transformation.

20 The transformation is clearly an "immediately useful" outcome of the method, as it can be used to convert gene expression signals into transformed gene expression signals, e.g., creating a uniform distribution of transformed gene expression signals.

The Examiner further argued that "there is no particular data identified or specific patterns recited in the specification such that a concrete, tangible, useful result is readily

25 apparent." *Id.* at page 3, 1st paragraph. Again Applicants respectfully disagree with the Examiner's assertions. As Applicants also highlighted in their previous response, the transformation may be used in discovering discriminative gene expression patterns. See, specification, page 14, lines 15-17.

Applicants further point out that, the present techniques teach that a control

30 matrix can be formed, the control matrix, e.g., containing a number of expressions from a number of experiments, each expression corresponding to how much or how little a particular

gene is being expressed. See, for example, page 12, lines 20-23, of the specification; FIG. 3. Transformations are then derived. Each transformation takes a probability density distribution for one column of the control matrix and transforms it to a uniform probability density. See, for example, page 14, lines 9-12, of the specification; FIG. 4. The transformations are applied to a

5   phenotype matrix. See, for example, page 14, lines 24-25, of the specification. Each entry in the phenotype matrix is an expression level of a particular gene. See, for example, page 14, line 20, of the specification; FIG. 5. The transformed value, as part of a transformed phenotype matrix, can be used to determine patterns. See, for example, page 14, line 27, through page 15, line 1, of the specification; FIG. 6.

10   Therefore, the present specification clearly provides a concrete, tangible, useful result, namely, the transformations. Further, to identify "particular data," as requested by the Examiner, one need only look, for example, to FIGS. 3-6, which clearly exemplify the teachings of the specification.

The Examiner further asserted in the final Office Action, page 3, 1st paragraph,

15   that "[t]he specification is devoid of information on a possible correlation of this method to a particular disease or disorder for which this method may be useful or a particular phenotype, for example. There is no recitation of what to do with the probabilities generated". Applicants respectfully disagree with the Examiner's assertions. The phenotype matrix, described above, e.g., has columns corresponding to particular genes and rows corresponding to particular

20   experiments. The experiments may be from cells that exhibit a certain disease phenotype, for example, cancer or diabetes. See, for example, page 14, lines 18-22, of the specification; FIG. 5. As described above, a transformed phenotype matrix can be used to determine patterns. Therefore, the specification clearly relates the present techniques to a "particular disease or disorder" or "a particular phenotype" for which the present methodology is useful.

25   Given the above remarks, Applicants respectfully request reconsideration and withdrawal of the rejections.

The Examiner also finally rejected claims 1-3, 17-19 and 23-25 under 35 U.S.C. §101 as allegedly lacking patentable utility. In the final Office Action, beginning on page 4, 3rd paragraph, the Examiner stated that,

The specification teaches that transformation of data can be used for identification of patterns in healthy versus unhealthy phenotypes such that these patterns may then be used to characterize an unknown sample into one of those two classes. However, the claimed method still is not directed to the steps of classifying unknown samples into phenotype groups. It is merely directed to transforming data that represent gene expression signals. . . Therefore the claimed method does not have utility. (internal citations omitted) (emphasis omitted)

Respectfully, Applicants disagree with the Examiner's assertions. First, Applicants submit that the present application has well established utility. For example, M.P.E.P. §2107 II. (A)(3) states that "[a]n invention has well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention . . . and (ii) the utility is specific, substantial, and credible." Applicants respectfully submit that the present teachings meet these requirements. The Examiner's arguments seem to agree with this conclusion (see Examiner's statements above regarding the teachings of the specification directed to, e.g., the classification of unknown samples), however the Examiner suggested that the <u>claimed</u> method does not have utility. Respectfully, Applicants find no support for the claim being the sole standard for utility under 35 U.S.C. §101. For this reason alone, Applicants respectfully request reconsideration and withdrawal of the rejection.

However, Applicants also submit that the present invention, as recited, e.g., in independent claims 1, 17 and 23, clearly has utility, namely, that of creating a uniform distribution of transformed gene expression signals. As such, Applicants respectfully request reconsideration and withdrawal of the rejections.

As mentioned above, the Examiner also finally rejected claims 1-3, 17-19 and 23-25 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Namely, the Examiner asserted that the phrase "transformation that renders uniform," appearing in claims 1, 17 and 23, remains unclear. The Examiner also asserted that the limitation of rendering uniform a probability distribution, as in claims 3, 19 and 25, is unclear. The Examiner further asserted that the term "mapped," as recited in claims 3, 19 and 25, is unclear. With regard to each of the above

rejections, Applicants have amended claims 1, 3, 17, 19, 23 and 25 and thus respectfully request reconsideration and withdrawal of the rejections.

PRIOR ART REJECTIONS

5   As mentioned above, the Examiner finally rejected claims 1-3, 17-19 and 23-25 under 35 U.S.C. §103(a) as allegedly unpatentable over Eisen. Applicants respectfully disagree with the Examiner's rejections for at least the reason that nowhere does Eisen teach or suggest deriving a transformation that creates, within a selected interval, a uniform distribution of transformed gene expression signals, as is required by independent claims 1, 17 and 23.

10   The Examiner pointed out that Eisen discloses intensity ratios that are transformed to treat inductions or repressions of identical magnitude. What Eisen in fact teaches is that values of a fluorescence ratio of experimental samples (Cy5) and reference samples (Cy3) "are log transformed . . . . to treat inductions or repressions of identical magnitude as numerically equal but with opposite signs." See Eisen, page 14864, 1st column. It appears that taking the log

15   of the ratio values allows the determination of which value, Cy5 or Cy3, is greater (e.g., a positive value indicating that Cy5 is greater than Cy3 and a negative value indicating that Cy5 is less than Cy3). Applicants fail to see how this teaching, in any way, makes obvious creating a uniform distribution of transformed gene expression signals. As such, Applicants respectfully request reconsideration and withdrawal of the rejections.
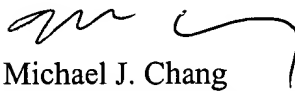
20   In view of the foregoing, the invention, as claimed in claims 1-3, 17-19 and 23-25, cannot be said to be taught or suggested by Eisen. Accordingly, Applicants submit that all of the pending claims, i.e., claims 1-3, 17-19 and 23-25, are in condition for allowance and such favorable action is earnestly solicited.

         If any outstanding issues remain, or if the Examiner has any further suggestions

25   for expediting allowance of this application, the Examiner is invited to contact the undersigned at the telephone number indicated below.

The Examiner's attention to this matter is appreciated.

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Respectfully submitted,

Date: July 16, 2004

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